VANM212001AUS

COPY OF PAPERS
ORIGINALLY FILED

PATENT

13/B
CJ
9/16/02
Ext(3)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Remacle, et al.	Group Art Unit 1634
Appl. No.	:	09/816,763	
Filed	:	March 23, 2001	
For	:	METHOD AND KIT FOR THE SCREENING, THE DETECTION AND/OR THE QUANTIFICATION OF TRANSCRIPTIONAL FACTORS	
Examiner	:	Chakrabarti, A.	

AMENDMENT

United States Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

In response to the Office Action mailed from the United States Patent and Trademark Office on March 15, 2002 (Paper No. 12), please amend the application as follows:

IN THE CLAIMS

Please cancel claims 11 and 35 without prejudice.

Please amend claims 1, 3, 5-8, 10, 12 and 34 as follows:

1. **(Amended)** A screening and/or quantification method of one or more transcriptional factors(s) present in a cell or cell lysate, said method comprising the steps of:

a. binding to an insoluble solid support double-stranded DNA sequence(s) at the concentration of at least 0.01 pmole/cm^2 of said solid support surface, said double-stranded DNA sequence comprising a specific sequence, said specific sequence being able to bind said one or more transcriptional factor(s) and said double-stranded DNA sequence being located from the surface of the solid support by a spacer corresponding to or comprising at least a double-stranded DNA nucleotide of at least 20 base pairs;

B1

b. putting into contact said one or more transcriptional factor(s) with said bound double-stranded DNA sequence(s); and

c. identifying and/or quantifying a signal resulting from the binding of said transcriptional factor(s) upon said double-stranded DNA sequence(s).

B1

3. **(Amended)** The method according to claim 1, wherein the specific sequence of the double-stranded DNA sequence(s) able to bind with the transcriptional factor(s) is located at a distance of at least about 6.8 nm from the surface of the solid support.

B2

5. **(Amended)** The method according to claim 1, wherein the signal resulting from the binding of the transcriptional factor upon the double-stranded DNA sequence is obtained through an enzymatic reaction.

6. **(Amended)** The method according to claim 1, for the screening and/or quantification of multiple different transcriptional factors present in a same biological sample.

B3

7. **(Amended)** The method according to claim 1, for the screening and/or quantification of transcriptional factors selected from the group consisting of NF-KB, AP-1, CREB, SP-1, C/EBP, GR, HIF-1, Myc, NF-AT, Oct, TBP, CBF-1 and factors listed in table 1.

8. **(Amended)** The method according to claim 1, for the screening and/or quantification of multiple different transcriptional factors upon a same support upon the same multiwell plate.

B4

10. **(Amended)** The method according to claim 1, wherein the spacer between the double-stranded DNA sequence(s) and the solid support is at least about 13.5 nm.

12. **(Amended)** The method according to claim 1, ~~wherein the binding of the~~ double-stranded DNA sequence(s) to the insoluble solid support is of non-covalent type and includes a binding pair comprising a first member and a second member, said first member being bound to the double-stranded DNA sequence, said second member being bound to the surface of the solid support.

B5

34. **(Amended)** The method of Claim 36, wherein said binding pair is biotin/streptavidin.

B6

Please add the following new claims:

36. **(New)** The method according to claim 12, wherein the binding pair is selected from the group consisting of biotin/streptavidin, hapten/receptor and antigen/antibody binding pair.

B7

37. **(New)** The method according to claim 1, wherein step b) comprises putting into contact said one or more transcriptional factor(s) in a cell lysate with said bound double-stranded DNA sequence(s).

38. **(New)** The method according to claim 1, wherein said spacer is a double-stranded DNA nucleotide sequence of at least 40 base pairs.

REMARKS

Claims 11 and 35 have been canceled without prejudice, claims 1, 3, 5-8, 10, 12 and 34 have been amended and new claims 36-38 have been added. Specific support for the amendment to claim 1 can be found in prior claims 10 and 11 and in the specification as filed on page 8, lines 11-13, page 8 lines 20-32, page 13, lines 1-10 and Examples 1-5. Support for the amendment to claim 12 is found in the specification as filed on page 11, lines 2-29 and within Example 1. Support for the amendment to claim 34 is found within prior claims 34 and 35. Claims 3, 5-8 and 10-12 were amended to correct minor informalities and establish antecedent basis. Accordingly, the amendments to claims 3, 5-8 and 10-12 do not narrow the scope of the claims. Specific support for new claim 36 is found in the specification as filed on page 11, lines 24-29, specific support for new claim 37 is found in claim 1, and specific support for new claim 38 is found within prior claim 11.

I. Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected Claims 1-22, 34 and 35 under 35 U.S.C. § 112, second paragraph on the assertion that the claims are indefinite in light of the recitation of such terms as "able to bind," "able to interact," "possibly," "preferably," and "6,8nm." Claims 1, 3, 5-8, 10-12 and 34 have been amended to remove the Examiner's concerns.

In light of the above remarks, Applicants respectfully request withdrawal of the rejection to the claims under 35 U.S.C. § 112, second paragraph.

II. Rejection under 35 U.S.C. § 102(b)

The Examiner has rejected Claims 1-8, 11-15, 17-22, 34 and 35 under 35 U.S.C. § 102(b) on the assertion that Peterson et al. (WO 95/30026, 11/9/95) anticipates the method embraced by the instant claims, namely a screening and/or quantification method of one or more transcriptional factor(s) present in a cell lysate.

In order for a reference to anticipate the claims, every element of the claimed invention must be taught by the cited reference. The present invention, as stated in claim 1 is directed to a screening method of one or more transcriptional factors(s) present in a cell or cell lysate, said method comprising the steps of:

a. binding to an insoluble solid support double-stranded DNA sequence(s) at the concentration of at least 0.01 pmole/cm^2 of said solid support surface, said double-stranded DNA sequence comprising a specific sequence, said specific sequence being able to bind said one or more transcriptional factor(s) and said double-stranded DNA sequence being located from the surface of the solid support by a spacer corresponding to or comprising at least a double-stranded DNA nucleotide of at least 20 base pairs;

b. putting into contact said one or more transcriptional factor(s) with said bound double-stranded DNA sequence(s); and

c. identifying and/or quantifying a signal resulting from the binding of said transcriptional factor(s) upon said double-stranded DNA sequence(s).

Peterson et al. do not teach a screening method of at least one transcriptional factor present in a cell or cell lysate using double-stranded DNA sequence(s) at a concentration of at least 0.01 pmole/cm^2 as recited in claim 1. Thus, Peterson et al. do not teach every element of the claimed invention as required by M.P.E.P. 2131.

In light of the above remarks, Applicants respectfully request withdrawal of the rejection to the claims under 35 U.S.C. § 102(b).

III. Rejection under 35 U.S.C. § 103(a)

Peterson et al.

The Examiner has rejected Claims 1-3, 6-15, 17-22, 34 and 35 under 35 U.S.C. § 103(a) on the assertion that Peterson et al. teach the method embraced by the instant claims.

According to M.P.E.P. 2143.03, all of the claimed limitations must be taught or suggested in the prior art. As discussed above, Peterson et al. does not teach or suggest all of the limitations recited in the claims.

Further, the method of the present invention allows for more sensitive detection of the transcription factor(s). As stated in the specification as filed on page 24, lines 8-33 and in figure 3 (purified p50), the method according to the present invention allows detection of the transcriptional factor(s) at concentrations of as low as 5×10^{-16} moles/well. According to Peterson et al., the range of transcriptional factor(s) is 10^{-9}M (see examples 1 to 7), equivalent to 10^{-13} moles/well. Thus, the present invention enables detection at a 100-fold lower concentration than those disclosed in Peterson et al.

Finally, according to M.P.E.P. 2143, objective evidence of unexpected results is relevant to the issue of obviousness. Here, there is an unexpected advantage involved in the order in which the components are added to the reaction mixture. In particular, in the present invention, the double-stranded DNA sequences are bound to the support prior to contact with the transcription factor. In contrast, page 12, line 31 to page 13, line 9 of Peterson et al. allows for any order of addition of the mixture components that provides the requisite binding. The binding of the double-stranded DNA molecules to the support prior to contacting the DNA with transcription factors enables the increased sensitivity disclosed in the instant application since the probability of the protein interacting with the DNA is lower in solution than in the case of DNA pre-immobilized on a solid support. Peterson et al. suggest forming a DNA-protein complex prior to immobilization of the DNA on the solid support (see pages 12-13 and examples). In the methods of Peterson et al., both DNAs (free and complexed to the transcription factors) will compete for binding to the support and the higher diffusion rate of the free (smaller) DNA will favor its binding to the support. Thus, the support will be saturated by the free DNA molecules. Thus, in contrast to the methods of Peterson, the present invention enables the screening and/or quantification of transcription factors at the concentration in which they exist in cells and cell lysates without requiring purification of the transcription factors.

For the foregoing reasons, Applicants respectfully submit that the claimed invention is not obvious over Peterson et al.

Peterson et al. in view of Voytas et al.

The Examiner has rejected Claims 1-3, 6-22, 34 and 35 over 35 U.S.C. § 103(a) on the assertion that it would have been obvious to combine the method of Peterson et al. with the HIV integrase transcriptional factor of Voytas et al. (USP 5,976,795, 11/2/99) in order to improve the screening process of transcription factors.

As stated above, the present invention is not taught or suggested by Peterson et al. The addition of the Voytas et al. reference which teaches the HIV integrase transcriptional

factor does not supplement the foregoing deficiencies in the Peterson reference to teach or suggest the claimed invention.

In view of the above remarks, Applicants respectfully request withdrawal of the rejection to the claims under 35 U.S.C. § 103(a).

IV. Conclusion

Claims 11 and 35 have been canceled without prejudice, claims 1, 3, 5-8, 10, 12 and 34 have been amended and new claims 36-38 have been added. The changes made to the claims by the current amendment, including insertions and **[deletions]**, are shown on an attached sheet entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this amendment. No new matter has been added herewith.

In view of the foregoing, Applicants respectfully submit the present application is fully in condition for allowance. If any issues remain that may be addressed by a phone conversation, the Examiner is invited to contact the undersigned at the phone number listed below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Dec. 3 2002

By: _____

Daniel Hart
Registration No. 40,637
Attorney of Record
2040 Main Street
Fourteenth Floor
Irvine, CA 92614
(619) 235-8550

O:\DOCS\MCM\MCM-2438.DOC - 070302